PENDING ORIGINAL CLAIMS; "NON-ELECTED" ORIGINAL CLAIMS WITHDRAWN PER RESTRICTION REQUIREMENT; ADDITION OF NEW CLAIMS

Please cancel claims 3 and 14 without prejudice.

Please cancel non-elected claims 15-18 and 20-22 without prejudice. Claims 15-18 and 20-22 are cancelled without prejudice pursuant to a restriction requirement as drawn to a non-elected invention and not for any reason related to patentability.

Claim 4 has been amended to depend from a non-cancelled claim and not for any reason related to patentability.

Claims 10 and 11 have been amended to delete unneeded SEQ ID NOS and not for any reason related to patentability.

new claims 23-109 are added.

1. (Original) A binding domain-immunoglobulin fusion protein, comprising:

(a) a binding domain polypeptide that is fused to an immunoglobulin hinge region polypeptide, wherein said hinge region polypeptide is selected from the group consisting of (i) a mutated hinge region polypeptide that contains no cysteine residues and that is derived from a wild-type immunoglobulin hinge region polypeptide having one or more cysteine residues, (ii) a mutated hinge region polypeptide that contains one cysteine residue and that is derived from a wild-type immunoglobulin hinge region polypeptide having two or more cysteine residues, (iii) a wild-type human IgA hinge region polypeptide, (iv) a mutated human IgA hinge region polypeptide that contains no cysteine residues and that is derived from a wild-type human IgA region polypeptide, and (v) a mutated human IgA hinge region polypeptide that contains one cysteine residue and that is derived from a wild-type human IgA region polypeptide;

(b) an immunoglobulin heavy chain CH2 constant region polypeptide that is fused to the hinge region polypeptide; and

(c) an immunoglobulin heavy chain CH3 constant region polypeptide that is fused to the CH2 constant region polypeptide,

wherein:

(1) the binding domain-immunoglobulin fusion protein is capable of at least one immunological activity selected from the group consisting of antibody dependent cell-mediated cytotoxicity and complement fixation, and

(2) the binding domain polypeptide is capable of specifically binding to an antigen.

2. (Original) The binding domain-immunoglobulin fusion protein of claim 1 wherein the immunoglobulin hinge region polypeptide is a mutated hinge region polypeptide and exhibits a reduced ability to dimerize, relative to a wild-type human immunoglobulin G hinge region polypeptide.

3. (Canceled)

4. (Amended) The binding domain-immunoglobulin fusion protein of claim ~~3~~ 1 wherein the immunoglobulin variable region polypeptide is derived from a human immunoglobulin.

5. (Original) The binding domain Fv-immunoglobulin fusion protein of claim 1 wherein the binding domain polypeptide comprises:

(a) at least one immunoglobulin light chain variable region polypeptide;

(b) at least one immunoglobulin heavy chain variable region polypeptide; and

(c) at least one linker peptide that is fused to the polypeptide of (a) and to the polypeptide of (b).

6. (Original) The binding domain-immunoglobulin fusion protein of claim 5 wherein the immunoglobulin light chain variable region and heavy chain variable region polypeptides are derived from human immunoglobulins.

7. (Original) The binding domain-immunoglobulin fusion protein of claim 1 wherein at least one of the immunoglobulin heavy chain CH2 constant region polypeptide and the immunoglobulin heavy chain CH3 constant region polypeptide is derived from a human immunoglobulin heavy chain.

8. (Original) The binding domain-immunoglobulin fusion protein of claim 1 wherein the immunoglobulin heavy chain constant region CH2 and CH3 polypeptides are of an isotype selected from the group consisting of human IgG and human IgA.

9. (Original) The binding domain-immunoglobulin fusion protein of claim 1 wherein the antigen is selected from the group consisting of CD19, CD20, CD37, CD40 and L6.

10. (Amended) The binding domain-immunoglobulin fusion protein of claim 5 wherein the linker polypeptide comprises at least one polypeptide having as an amino acid sequence Gly-Gly-Gly-Gly-Ser ~~[SEQ ID NO:21]~~.

11. (Amended) The binding domain-immunoglobulin fusion protein of claim 5 wherein the linker polypeptide comprises at least three repeats of a polypeptide having as an amino acid sequence Gly-Gly-Gly-Gly-Ser ~~[SEQ ID NO:21]~~.

12. (Original) The binding domain-immunoglobulin fusion protein of claim 1 wherein the immunoglobulin hinge region polypeptide comprises a human IgA hinge region polypeptide.

13. (Original) The binding domain-immunoglobulin fusion protein of claim 1 wherein the binding domain polypeptide comprises a CD154 extracellular domain.

14-18 (Canceled)

19. (Original) A pharmaceutical composition comprising a binding domain-immunoglobulin fusion protein according to claim 1 in combination with a physiologically acceptable carrier.

20-22. (Canceled)

Please add the following new claims:

23. (New) A single chain protein, comprising:

(a) a binding domain polypeptide capable of binding to a cellular target, said binding domain polypeptide being joined to

(b) a hinge peptide, said hinge peptide being joined to

(c) an immunoglobulin heavy chain CH2 constant region polypeptide, said CH2 constant region polypeptide being joined to

(d) an immunoglobulin heavy chain CH3 constant region polypeptide,

wherein said hinge peptide is an IgG or IgA hinge peptide that contains one or two cysteine residues, provided that when the hinge peptide contains two cysteines the first cysteine of the hinge that is responsible for forming a disulfide bond with a light chain constant region in a naturally-occuring IgG or IgA antibody is not deleted or substituted with an amino acid, and

wherein said single chain protein (1) is capable of binding to said target, and (2) is capable of antibody dependent cell-mediated cytotoxicity and complement fixation, and (3) is capable of decreasing the number of target cells.

24. (New) A single chain protein, comprising:

(a) a binding domain polypeptide capable of binding to a cellular target, said binding domain polypeptide being joined to

(b) a hinge peptide, said hinge peptide being joined to

(c) an immunoglobulin heavy chain CH2 constant region polypeptide, said CH2 constant region polypeptide being joined to

(d) an immunoglobulin heavy chain CH3 constant region polypeptide,

wherein said single chain protein (1) is capable of binding to said target, and (2) is capable of antibody dependent cell-mediated cytotoxicity and complement fixation, and (3) is capable of decreasing the number of target cells.

25. (New) A single chain protein, comprising:

(a) a binding domain polypeptide capable of binding to a cellular target, said binding domain polypeptide being joined to

(b) a hinge peptide, said hinge peptide being joined to

(c) an immunoglobulin heavy chain CH2 constant region polypeptide, said CH2 constant region polypeptide being joined to

(d) an immunoglobulin heavy chain CH3 constant region polypeptide,

wherein said single chain protein is capable of binding to said target and decreasing the number of target cells.

26. (New) The single chain protein of either of claims 23, 24, or 25 wherein said binding domain polypeptide is a single chain Fv polypeptide.

27. (New) The single chain protein of any one of claims 23, 24, 25, or 26 wherein said single chain protein is capable of binding to a B cell target.

28. (New) The single chain protein of claim 27 wherein said B cell target is CD20.

29. (New) The single chain protein of claim 27 wherein said B cell target is CD37.

30. (New) The single chain protein of claim 27 wherein said B cell target is selected from the group consisting of CD19, CD22, CD30 ligand, CD54, CD106, and interleukin-12.

31. (New) The single chain protein of claim 27 wherein said single chain protein is capable of depleting a population of target cells.

32. (New) The single chain protein of claim 27 wherein said single chain protein is capable decreasing the number of target cells in vivo.

33. (New) The single chain protein of claim 27 wherein said single chain protein is capable decreasing the number of target cells in vitro.

34. (New) The single chain protein of any of claim 26 wherein the heavy and light chain variable regions of the scFv are joined by a polypeptide linker of at least about 6 amino acids.

35. (New) The single chain protein of claim 26 wherein said single chain Fv polypeptide is capable of binding to a target selected from the group consisting of CD2, CD5,

CD10, CD27, CD28, CD40, CTLA-4, 4-1BB, 4-1BB ligand,interferon-γ, interleukin-4, interleukin-17, and interleukin-17 receptor.

36. (New) The single chain protein of claim 26 wherein said single chain Fv polypeptide is capable of binding to a target selected from the group consisting of CD59, CD48, CD72, CD70, CD86/B7.2, CD40 ligand, IL-17, CD43 and VLA-4 ($\alpha_4\beta_7$).

37. (New) The single chain protein of claim 26 wherein said single chain Fv polypeptide is capable of binding to a target selected from the group consisting of CD83 and DEC-205.

38. (New) The single chain protein of claim 26 wherein said single chain Fv polypeptide is capable of binding to a target selected from the group consisting of HER1, HER2, HER3, HER4, epidermal growth factor receptor, vascular endothelial cell growth factor, vascular endothelial cell growth factor receptor, insulin-like growth factor-I, insulin-like growth factor-II, transferrin receptor, estrogen receptor, progesterone receptor, follicle stimulating hormone receptor, retinoic acid receptor, MUC-1, NY-ESO-1, NA 17-A, Melan-A/MART-1, tyrosinase, Gp-100, MAGE, BAGE, GAGE, any of the CTA class of receptors including in particular HOM-MEL-40 antigen encoded by the SSX2 gene, carcinoembyonic antigen, and PyLT.

39. (New) The single chain protein of any of claims 23-26 wherein said target is CD20 and said binding domain is capable of binding CD20, wherein said hinge peptide contains one or more serine residues in place of one or more cysteine residues, and wherein said immunoglobulin heavy chain CH2 and CH3 constant region polypeptides are are IgG1 CH2 and CH3 constant region polypeptides.

40. (New) The single chain protein of claim 39, wherein said single chain protein includes a 2H7 single chain Fv binding domain polypeptide.

41. (New) The single chain protein of claim 39, wherein said single chain protein includes a 2H7 single chain Fv binding domain polypeptide, and wherein said hinge peptide contains one or more serine residues in place of one or more cysteine residues.

42. (New) The single chain protein of any of claims 23-26, wherein said target is CD20 and said binding domain is capable of binding CD20, wherein said hinge peptide contains one or more serine residues in place of one or more cysteine residues, and wherein said heavy chain constant region comprises a CH2 domain in which a leucine has been replaced with serine at position 234.

43. (New) The single chain protein of claim 42, wherein the binding domain polypeptide in said single chain protein is a 2H7 single chain Fv, and wherein said hinge peptide contains one or more serine residues in place of one or more cysteine residues.

44. (New) The single chain protein of claim 42 wherein said single chain Fv polypeptide is a 2H7 single chain Fv, and wherein said hinge peptide comprises at least a portion of an IgA hinge.

45. (New) The single chain protein of claim 44 wherein said hinge peptide comprises a wild type IgA hinge.

46. (New) The single chain protein of any of claims 23-26 wherein said target is a L6 carcinoma antigen, said binding domain is capable of binding L6, said hinge peptide comprises

at least a portion of an IgA hinge, and said immunoglobulin heavy chain CH2 and CH3 constant region polypeptides are IgG1 CH2 and CH3 constant region polypeptides .

47. (New) The single chain protein of claim 46 wherein said hinge peptide comprises a wild type IgA hinge.

48. (New) The single chain protein of any of claims 23-26 wherein said target is a L6 carcinoma antigen, said binding domain is capable of binding L6, said hinge peptide contains one or more serine residues in place of one or more cysteine residues, and said immunoglobulin heavy chain CH2 and CH3 constant region polypeptides are are IgG1 CH2 and CH3 constant region polypeptides.

49. (New) The single chain protein of claim 48 wherein said hinge peptide contains three serine residues in place of three cysteine residues.

50. (New) A pharmaceutical composition comprising a single chain protein according to any one of claims 1, or 23-26 in combination with a physiologically acceptable carrier in a form suitable for administration in an amount useful for the treatment of a malignant condition or B-cell disorder in a patient.

51. (New) A pharmaceutical composition of claim 50 wherein said single chain protein target is CD20 and is capable of binding CD20 with a binding affinity of at least about 10^7 M^{-1}.

52. (New) A pharmaceutical composition of claim 50 wherein said single chain protein comprises a single chain Fv selected from the group consisting of 2H7 single chain Fvs, L6 single chain Fvs, HD37 single chain Fvs, and G28-1 single chain Fvs.

53. (New) A pharmaceutical composition of claim 52 wherein said single chain protein target is CD20 and said single chain Fv is capable of binding CD20, wherein said single chain Fv is not a 1F5 single chain Fv.

54. (New) A pharmaceutical composition of claim 52 wherein said single chain protein target is CD20 and said single chain Fv is a 2H7 single chain Fv.

55. (New) A pharmaceutical composition of claim 52 wherein said single chain Fv polypeptide is capable of binding to a B cell target.

56. (New) A pharmaceutical composition of claim 55 wherein said B cell target is CD20.

57. (New) A pharmaceutical composition of claim 55 wherein said B cell target is CD37.

58. (New) A pharmaceutical composition of claim 55 wherein said B cell target is selected from the group consisting of CD19, CD22, CD30 ligand, CD54, CD106, and interleukin-12.

59. (New) A pharmaceutical composition of any of claims 50-58 wherein the binding domain polypeptide of said single chain protein comprises a heavy chain variable region and a light chain variable region, wherein said heavy and light chain variable regions of the scFv are joined by a polypeptide linker of at least about 6 amino acids.

60. (New) A pharmaceutical composition of claim 50 wherein the binding domain polypeptide of said single chain protein comprises a single chain Fv polypeptide capable of

binding to a target selected from the group consisting of CD2, CD5, CD10, CD27, CD28, CD40, CTLA-4, 4-1BB, 4-1BB ligand, interferon-γ, interleukin-4, interleukin-17, and interleukin-17 receptor.

61. (New) A pharmaceutical composition of claim 50 wherein the binding domain polypeptide of said single chain protein comprises a single chain Fv polypeptide capable of binding to a target selected from the group consisting of CD59, CD48, CD72, CD70, CD86/B7.2, CD40 ligand, IL-17, CD43 and VLA-4 ($\alpha_4\beta_7$).

62. (New) A pharmaceutical composition of claim 50 wherein the binding domain polypeptide of said single chain protein comprises a single chain Fv polypeptide capable of binding to a target selected from the group consisting of CD83 and DEC-205.

63. (New) A pharmaceutical composition of claim 50 wherein said binding domain polypeptide of said single chain protein comprises a single chain Fv polypeptide capable of binding to a target selected from the group consisting of HER1, HER2, HER3, HER4, epidermal growth factor receptor, vascular endothelial cell growth factor, vascular endothelial cell growth factor receptor, insulin-like growth factor-I, insulin-like growth factor-II, transferrin receptor, estrogen receptor, progesterone receptor, follicle stimulating hormone receptor, retinoic acid receptor, MUC-1, NY-ESO-1, NA 17-A, Melan-A/MART-1, tyrosinase, Gp-100, MAGE, BAGE, GAGE, any of the CTA class of receptors including in particular HOM-MEL-40 antigen encoded by the SSX2 gene, carcinoembyonic antigen, and PyLT.

64. (New) A pharmaceutical composition of claim 50 wherein the hinge peptide of said single chain protein is a naturally-occurring immunoglobulin hinge region polypeptide.

65. (New) A pharmaceutical composition of claim 64 wherein said naturally-occurring immunoglobulin hinge region polypeptide is an IgG1 hinge region polypeptide.

66. (New) A pharmaceutical composition of claim 65 wherein said IgG1 hinge region polypeptide is a human IgG1 hinge region polypeptide.

67. (New) A pharmaceutical composition of claim 64 wherein said naturally-occurring immunoglobulin hinge region polypeptide is an IgD hinge region polypeptide.

68. (New) A pharmaceutical composition of claim 64 wherein said naturally-occurring immunoglobulin hinge region polypeptide is selected from the group consisting of an IgG2 hinge region polypeptide, an IgG3 hinge region polypeptide, and an IgG4 hinge region polypeptide.

69. (New) A pharmaceutical composition of claim 68 wherein said IgG2, IgG3 and IgG4 hinge region polypeptides are human IgG2, IgG3 and IgG4 hinge region polypeptides.

70. (New) A pharmaceutical composition of claim 64 wherein said naturally-occurring immunoglobulin hinge region polypeptide is an IgA hinge region polypeptide.

71. (New) A pharmaceutical composition of claim 70 wherein said IgA hinge region polypeptide is a human IgA hinge region polypeptide.

72. (New) A pharmaceutical composition of claim 50 wherein the hinge peptide of said single chain protein is mutated naturally-occurring immunoglobulin hinge region polypeptide.

73. (New) A pharmaceutical composition of claim 72 wherein said naturally-occurring immunoglobulin hinge region polypeptide is human.

74. (New) A pharmaceutical composition of claims 72 or 73 wherein said mutated hinge region polypeptide has been altered to contain less cysteine amino acid residues than the naturally-occurring immunoglobulin hinge region polypeptide from which it was derived.

75. (New) A pharmaceutical composition of claims 72 or 73 wherein said mutated immunoglobulin hinge region polypeptide has two cysteine amino acid residues.

76. (New) A pharmaceutical composition of claim 71 wherein said mutated immunoglobulin hinge region polypeptide is an IgG hinge region polypeptide having two cysteine amino acid residues.

77. (New) A pharmaceutical composition of claims 72 or 73 wherein said mutated immunoglobulin hinge region polypeptide has one cysteine amino acid residue.

78. (New) A pharmaceutical composition of claims 72 or 73 wherein said mutated immunoglobulin hinge region polypeptide has no cysteine amino acid residues.

79. (New) A pharmaceutical composition of claim 77 wherein said mutated immunoglobulin hinge region polypeptide is an IgG hinge region polypeptide having one cysteine amino acid residue.

80. (New) A pharmaceutical composition of claim 77 wherein said mutated immunoglobulin hinge region polypeptide is an IgG1 hinge region polypeptide having one cysteine amino acid residue and wherein said cysteine amino acid residue is not the IgG1 hinge

region cysteine residue responsible for forming a disulfide bond with a light chain cysteine residue.

81. (New) A pharmaceutical composition of claim 77 wherein said mutated immunoglobulin hinge region polypeptide is an IgA hinge region polypeptide having one cysteine amino acid residue.

82. (New) A pharmaceutical composition of claim 78 wherein said mutated immunoglobulin hinge region polypeptide is an IgG hinge region polypeptide having no cysteine amino acid residues.

83. (New) A pharmaceutical composition of claim 78 wherein said mutated immunoglobulin hinge region polypeptide is an IgA hinge region polypeptide having no cysteine amino acid residues.

84. (New) A pharmaceutical composition of claim 50 wherein the hinge peptide of said single chain protein is selected from the group consisting of naturally occurring immunoglobulin hinge region polypeptides and mutated immunoglobulin hinge region polypeptides.

85. (New) A pharmaceutical composition of claim 84 wherein said hinge peptide is from about 5 to about 65 amino acids.

86. (New) A pharmaceutical composition of claim 84 wherein said hinge peptide is from about 10 to about 50 amino acids.

87. (New) A pharmaceutical composition of claim 84 wherein said hinge peptide is from about 15 to about 35 amino acids.

88. (New) A pharmaceutical composition of claim 84 wherein said hinge peptide is from about 18 to about 32 amino acids.

89. (New) A pharmaceutical composition of claim 84 wherein said hinge peptide is from about 20 to about 30 amino acids.

90. (New) A pharmaceutical composition of any of claims 85-89, wherein said hinge peptide further comprises one or more C-terminal CH1 domain amino acids.

91. (New) A pharmaceutical composition of any of claims 85-89, wherein said hinge peptide further comprises one or more C-terminal CH2 domain amino acids.

92. (New) A pharmaceutical composition of claim 50 wherein said immunoglobulin heavy chain CH2 constant region polypeptide is an IgG heavy chain CH2 constant region polypeptide.

93. (New) A pharmaceutical composition of claim 50 wherein said immunoglobulin heavy chain CH3 constant region polypeptide is an IgG heavy chain CH3 constant region polypeptide.

94. (New) A pharmaceutical composition of claims 92 or 93 wherein said constant region polypeptides are human constant region polypeptides.

95. (New) A pharmaceutical composition of claim 50 wherein said immunoglobulin heavy chain CH2 constant region polypeptide is an IgA heavy chain CH2 constant region polypeptide.

96. (New) A pharmaceutical composition of claim 50 wherein said immunoglobulin heavy chain CH3 constant region polypeptide is an IgA heavy chain CH3 constant region polypeptide.

97. (New) A pharmaceutical composition of claims 95 or 96 wherein said constant region polypeptides are human constant region polypeptides.

98. (New) A pharmaceutical composition of claim 50 wherein said target is CD20 and said binding domain is capable of binding CD20, one or more cysteine residues in said hinge peptide have been replaced with one or more serine residues, and said immunoglobulin heavy chain CH2 and CH3 constant region polypeptides are from IgG1.

99. (New) A pharmaceutical composition of claim 98, wherein said single chain protein is a 2H7 single chain Fv, and one or more cysteine residues in said hinge peptide have been replaced with one or more serine residues.

100. (New) A pharmaceutical composition of claim 50 wherein said target is CD20, said binding domain is capable of binding CD20, one or more cysteine residues in said hinge peptide have been replaced with one or more serine residues, and wherein said heavy chain constant region comprises a CH2 domain where leucine is substituted with serine at position 234.

101. (New) A pharmaceutical composition of claim 99, wherein said single chain protein is a 2H7 scFv in which three cysteine residues in said hinge peptide are substituted with serine.

102. (New) The single chain protein of claim 26 wherein said single chain Fv polypeptide is a 2H7 scFv, wherein said hinge peptide comprises at least a portion of an IgA hinge.

103. (New) The single chain protein of claim 102 wherein said hinge peptide comprises a wild type IgA hinge.

104. (New) The single chain protein of claim 26 wherein said target is an L6 carcinoma antigen, said binding domain is capable of binding L6, said hinge peptide comprises at least a portion of an IgA hinge, and said immunoglobulin heavy chain CH2 and CH3 constant region polypeptides are from IgG1.

105. (New) The single chain protein of claim 104 wherein said hinge peptide comprises a wild type IgA hinge.

106. (New) The single chain protein of claim 26 wherein said target is an L6 carcinoma antigen, said binding domain is capable of binding L6, one or more cysteine residues in said hinge peptide have been replaced with one or more serine residues, and said immunoglobulin heavy chain CH2 and CH3 constant region polypeptides are from IgG1.

107. (New) A single chain protein comprising a binding domain polypeptide capable of binding to CD20 joined to an IgE constant region polypeptide.

108. (New) A single chain protein of claim 107 wherein said IgE constant region comprises two or three IgE constant region domains.

109. (New) A pharmaceutical composition according to claim 50 wherein said malignant condition or a B-cell disorder is selected from the group consisting of rheumatoid arthritis, myasthenia gravis, Grave's disease, type I diabetes mellitus, multiple sclerosis and an autoimmune disease.